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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/654,276	09/01/2000	Smadar Cohen	9124.117US01	5848

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EXAMINER	
WEHBE, ANNE MARIE SABRINA	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 08/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/654,276	COHEN ET AL.	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5,6,9,10 and 16-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 5-6, 9-10, and 16-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/9/04 has been entered. Applicant's amendment filed on 6/9/04 has also been entered. New claims 22-24 have been added. Claims 1-3, 5-6, 9-10, and 16-24 are currently pending and under examination in the instant application. An action on the merits follows.

Those sections of Title 35, US code, not included in the instant action can be found in the previous office action.

Claim Rejections - 35 USC § 112

The rejection of claims pending claims 1-3, 5-6, 9-10, and 16-24 under 35 U.S.C. 112, first paragraph, for scope of enablement is maintained in part. Applicant's arguments have been fully considered but have not been found persuasive in overcoming the following grounds of rejection for reasons of record as discussed in detail below.

The applicant has amended the claims to limit the mammalian cells growing on the three-dimensional porous polysaccharide matrix to cardiomyocytes or cardiomyocytes in combination

with fibroblasts, endothelial cells, or smooth muscle cells. This amendment has obviated the previous grounds of rejection concerning the lack of enablement for practicing the claimed method in the absence of cardiomyocytes.

The sole remaining grounds of rejection concerns the lack of enabling disclosure for using allogeneic or xenogeneic adult cardiomyocytes alone or in combination with allogeneic or xenogeneic adult fibroblasts, endothelial cells, or smooth muscle cells in the instant invention. The previous office action provided the following scope of enablement: the specification provides an enabling disclosure for growing fetal or autologous cardiomyocytes alone or in the presence of fetal or autologous endothelial cells, fibroblasts, or smooth muscle cells on an alginate scaffold and using the resulting biografts to treat cardiac damage.

The applicant argues that limitation to fetal cells or autologous cells is not necessary because the art at the time of filing taught immunosuppressive drugs which could be used to prevent rejection of transplanted allogeneic tissue, citing Superdock and Helderman, and Woodley et al. Based on the knowledge in the prior art, the applicant argues that the enablement requirement has been met, citing *Bayer AG v. Schein Pharmaceuticals*.

In response, the office points out that the claims as amended read allogeneic or xenogeneic adult cardiomyocytes alone or in combination with allogeneic or xenogeneic adult fibroblasts, endothelial cells, or smooth muscle cells. Further, claims directed to cardiomyocytes and a second population of cells do not place any limitation on whether the origin of the second cell type is the same or different from the origin of the cardiomyocytes. Thus, the claims read for example on allogeneic cardiomyocytes and xenogeneic fibroblasts, or allogeneic cardiomyocytes from a first individual and allogeneic fibroblasts from a second individual. As discussed in detail

in the previous office actions, non-autologous adult tissue is subject to substantial allogeneic or xenogeneic immune responses which severely limit the ability of the cells to survive in the host and render any therapeutic benefit (Li et al. and Kaufman et al.) In particular, transplantation of xenogeneic tissue results in hyperacute rejection caused by preformed anti-xeno antibodies (Kaufman et al.). While Superdock and Helderman, and Woodley et al. provide some guidance for suppression of allogeneic immune responses using immunosuppressive drug regimens, these articles are silent in regards to preventing hyperacute rejection of xenogeneic tissue. Since the antibodies are present naturally, immunosuppressive drugs would have no effect on their activity. In addition, the previous office actions pointed out that the specification does not provide any guidance as to measures or methods necessary to prevent destructive allogeneic or xenogeneic immune responses following the transplantation of the matrix containing allogeneic or xenogeneic or a combination of the two to a subject. As stated in the previous office action, the Federal circuit has ruled:

....a specification need not disclose what is well known in the art. See, e.g., Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). **However**, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, **when there is no disclosure** of any specific starting material **or of any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art**. It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement.
Genentech Inc. v. Novo Nordisk A/S, 42 USPQ2d 1005 (CAFC 1997) (emphasis added).

Thus, applicant's argument that all the disclosure necessary to allow the use of adult allogeneic or xenogeneic cells in the instant invention is present in the prior art is found unpersuasive.

Regarding applicant's citation of *Bayer AG v. Shein Pharmaceuticals* , this piece of case law does not appear to be on point. *Bayer AG v. Shein Pharmaceuticals* discusses the "best mode" requirement of 35 U.S.C. 112, first paragraph. The instant rejection is an enablement rejection, not a "best mode" rejection. Further, the fact pattern in *Bayer AG v. Shein Pharmaceuticals* concerns whether a parent specification disclosed the best mode for making an unclaimed intermediate when the claims were directed to a final product. This is not analogous to the instant rejection or the instant claims. Furthermore, the citation of MPEP 2164.08 is confusing, since this section of the MPEP discusses single means claims, the presence of inoperable embodiments, and critical features not claimed. It is assumed that the applicant is relying on the section concerning "critical features not claimed", however this is not the issue in the instant rejection. The MPEP discusses situations where a critical feature is discussed in the specification which is not present in the claims. In the instant situation, the specification does not provide any guidance for preventing anti-allogeneic or anti-xenogeneic immune responses.

Therefore, for the reasons of record discussed in detail above, the rejection of claims 1-3, 5-6, 9-10, and 16-24 stands.

No claims are allowed.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action

after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. The examiner can be reached Monday- Friday from 10:30-7:00 EST. If the examiner is not available, the examiner's supervisor, Amy Nelson, can be reached at (571) 272-0804. For all official communications, the technology center fax number is (703) 872-9306. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737.

Dr. A.M.S. Wehbé

NE M. WEHBE' PH.D
ARY EXAMINER